AIDS
MEMORANDUM
Acquired Immune Deficiency Syndrome

National Institute of Allergy and Infectious Diseases

Volume 1, Number 4 April 1984

IN THIS ISSUE

GROUND RULES FOR USE OF THE AIDS MEMORANDUM

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ETHICAL AND LEGAL ISSUES IN THE PREVENTION AND TREATMENT OF AIDS

This article is an excerpt of a paper presented at a conference on AIDS in October 1983.

1. Responsibilities to AIDS Patients

These remarks presuppose that there is no clear evidence for the transmission of AIDS through casual contact.

The first moral obligation of health professionals to AIDS patients may seem self-evident, but it is not, either in practice or in some major codes of professional ethics. It is the obligation to treat AIDS patients.

There have been anecdotal reports of instances in which health professionals have refused to become involved with AIDS victims. The primary motive for such actions is no doubt fear, but there may be included in the refusals the sentiment that "After all, they have brought the problem on themselves." I will address first the sentiment, then the fear.

The sentiment clearly does not apply to all AIDS patients. In their AIDS report of October 17, 1983, the CDC noted that 16 hemophiliacs not known to be members of other high-risk groups have contracted AIDS. In addition, there are 157 US cases of AIDS in which the risk factors causing the disease are either anomalous or unknown. Thus, for approximately 7% of AIDS patients in the US, the assertion that "They have brought the problem on themselves" is likely to be both untrue and unfair.

But what about the 72% of AIDS patients who are male homosexuals or bisexuals and the 17% who are intravenous drug users? They fall within the much larger category of persons in our society whose lifestyles are or may be significant factors in their health status. (It should be noted, however, that the earliest victims of AIDS could not have known that their style of life placed them at greater risk for such a devastating disease.) But if we are going to consider voluntary risks to health as criteria for health-care eligibility, then the discussion should be broadened to include not just AIDS, and not just the sexually transmitted diseases, but rather a wide variety of lifestyle factors. For example, in a standard public health textbook, the following behavioral factors are listed as risks to health: smoking, alcohol and drug abuse, nutritional abuse, lack of adequate physical activity, motor vehicle accidents, violence, lack of adequate family supports, sexual promiscuity and contraceptive carelessness, and excessive television viewing (Somers AR: in Last JM (Ed): Maxcy-Rosenau Public Health and Preventive Medicine, 11th ed., Appleton Century Crofts, New York, 1980, 1046-1065). Thus, the watchwords should probably be "We have brought many problems on ourselves," rather than "They have brought the problem on themselves." Health professionals who prefer not to treat self-induced morbidity should probably begin by refusing to help heavy smokers who develop lung cancer or teenage drivers whose speeding results in their being critically injured.

It is the obligation of health professionals to treat all patients who seek their aid without regard to the causes of the patients' illnesses or injuries. But what can be said about the other concern--perhaps the major concern--that AIDS patients constitute a threat to the health of their caretakers? There is no clear evidence that AIDS has ever been transmitted from a patient to a member of a health care

team (Morb Mort Weekly Rep., 1983, 32 (27):358-360).

In contrast, there is clear positive evidence that several other diseases are regularly spread from patients to their caretakers (for example, Berman J, Levin ML, Orr ST, et al: Am J Public Health, 1981, 71(11):217-222; Ahlfors K, Ivarsson SA, Johnsson T, et al: Acta Paediatr Scand., 1981, 70(6):819-823; Platonov SA, Orgel MI, Matoshko GV, et al: Vrach Delo., 1981, 11:107-110). In 1981 Yale-New Haven Hospital reported that, between 1972 and 1979, 34 of its employees contracted hepatitis B while fulfilling their health-related duties. The incidence of occupational disease was highest among persons administering venipunctures, followed by emergency room personnel, members of the dialysis unit, housestaff, laboratory personnel, nurses, and support service personnel (Pantelick EL, Steere AC, Lewis HD, et al: Am J Med., 1981, 70(4):924-927). In short, health care professionals knowingly accept a small risk of contracting several diseases from patients; but, as far as is known, AIDS is not one of those diseases.

Since the epidemiology of AIDS seems to be similar to that of hepatitis B, it is conceivable that at some point in the future a health care professional will contract AIDS through an accidental needlestick or through contact with tissues or fluids from an AIDS patient. Should health professionals accept such a hypothetical risk for the sake of their patients?

From a legal standpoint, a physician has no obligation to help any particular patient (Holder AR: Medical Malpractice Law, 2nd ed., John Wiley and Sons, New York, 1978, 7-19). Further, legally speaking, a private hospital is generally obliged to provide only emergency care; it need not accept a seriously ill patient for long-term care (Warren DG: Problems in Hospital Law, 3rd ed., Aspen Systems Corp., Germantown, Maryland, 1978, 81-91).

Even in the major codes of professional ethics, there is apparent hesitation to acknowledge a general duty to care for the ill. The American Medical Association's Principles of Medical Ethics (1980) asserts that, except in emergencies, "A physician shall, in the provision of appropriate patient care, ... be free to choose whom to serve ..." (reprinted in Beauchamp TL, Walters L: Contemporary Issues in Bioethics, 2nd ed., Wadsworth Publishing Co., Belmont, California, 1982, 122). Similarly, the 1976 Code for Nurses of the American Nurses' Association (ANA) also qualifies the duty to treat: "If personally opposed to the delivery of care in a particular case because of the nature of the health problem or the procedures to be used, the nurse is justified in refusing to participate" (Ibid: 123). The nurses' right of conscientious refusal applies in all nonemergency situations.

However, other parts of the nurses' code and the great tradition of professional practice point toward a general moral duty to provide care to anyone who needs it, despite potential risks to one's own health. Thus, the ANA Code begins with the declaration that "The nurse provides services with respect for human dignity and the uniqueness of the client unrestricted by considerations of social and economic status, personal attributes, or the nature of the health problem." In her Notes on Nursing, published in 1860, Florence Nightingale was even more explicit about the moral duty to care. She wrote: "True nursing ignores infection, except to prevent it.

Cleanliness and fresh air from open windows, with unremitting attention to the patient, are the only defence a true nurse either asks or needs" (Nightingale F: Notes on Nursing: What It Is, and What It Is Not, Dover Publications, New York, 1969, 33-34). The medical profession also has its examples of physicians exemplifying profiles in courage (Eisenberg L: Science, 1977, 198(4322): 1105-1110; Barrett-Connor E: JAMA, 1979, 241 (1):37).

Thus, despite the hesitation evident in two recent codes of professional ethics, the history of health care theory and practice lends strong support to what might be called the altruistic thesis--namely, that health professionals have a moral duty to care for all who need their help. This responsibility holds even if many AIDS patients, like many patients with other serious diseases, have contributed to the compromise of their good health. This moral duty to provide care will remain a duty even if the transmission of AIDS from a patient to a physician, nurse, or clinical laboratory worker is one day documented.

In addition to the general duty to provide care for AIDS patients, health professionals have specific moral duties which are of great importance to AIDS patients. I will briefly mention two: the duty to respect privacy and the duty to provide appropriate care for the dying.

All of the major codes of health-care ethics stress the obligation of health professionals to preserve the confidentiality of information that passes from patients to their caregivers. The duty of confidentiality is especially important when sensitive information about sexual practices or drug use is elicited from patients for diagnostic or therapeutic purposes.

One legal step that has been taken by some government agencies involves the provision of a protective "shield" for sensitive medical information. In New York City, for example, medical records concerning drug abuse, sexually transmitted diseases, and AIDS are immune to subpoena (D. Lorimer, personal communication). Similar legislation has been enacted at the federal level to protect the confidentiality of health information gathered by the National Center for Health Statistics (U. S. Code, Title 42, Paragraph 242m(d)).

A second specific duty of health professionals is to provide appropriate care for patients who are in the terminal stages of their disease. Many AIDS patients die a lingering death in the hospital, sometimes after having lost contact with their social support systems. As ethicist Paul Ramsey has so eloquently reminded us, health professionals have an ongoing responsibility to care for the dying, even when all possibility of cure is gone (Ramsey P: in The Patient as Person, Yale University Press, New Haven, 1970, 113-164). Similarly, the great English clinician, Thomas Percival, made the point in his Medical Ethics, published in 1803, that "the offices of a physician may continue to be highly useful to the patient and comforting to the relatives around him, even in the last period of a fatal malady; by obviating despair, by alleviating pain, and by soothing mental anguish" (Percival T: in Leake CD (Ed): Percival's Medical Ethics, Williams & Wilkins, Baltimore, 1927, 98).

II. Responsibilities to Other Members of the Society

Contrary to popular mythology, AIDS is not likely to be spread through casual contact with AIDS patients. Since AIDS seems to be transmitted sexually or

through blood or blood products, there are three major groups at risk of contracting AIDS from AIDS patients: (1) their sexual partners, if any; (2) persons who share needles with AIDS patients, if the patients use intravenous drugs; and (3) persons receiving blood or blood products donated by AIDS patients. The public health dimension of AIDS is complicated by uncertainty about the absolute levels of risk for these three groups and by uncertainty about whether persons who have latent AIDS without major clinical symptoms can transmit the disease to others.

It can be argued that the close personal associates of a patient who has clinically demonstrated AIDS (groups 1 and 2 above) have a moral right to know about the patient's condition. This right would be based on the life-threatening character of AIDS, the possibility of transmitting the disease from patient to associate through sexual contact or shared needles, and the possibility of reducing the relative risk of such transmission. Even if this moral right to know is granted to the patient's associates, there remains a critical question: Who has the corresponding moral duty to inform those associates?

Here one despairs of formulating a general rule to cover all cases. However, in a society that is as committed to individual civil liberties as we profess to be, the preference should go to voluntaristic approaches that rely on (a) the concern of AIDS patients for their associates and (b) the information that members of high-risk groups have received and will receive from carefully targeted public education programs. This voluntaristic approach can be combined with the mandatory reporting of AIDS cases for surveillance purposes, provided that personal identifiers are removed from case reports to protect the anonymity of individual patients.

The third group at possible risk of contracting AIDS from AIDS patients is comprised of distant neighbors, the recipients of blood or blood products donated by AIDS patients, or perhaps even by future AIDS patients who have not yet developed frank disease. As noted earlier, there are 16 hemophiliacs who are not known to be members of high-risk groups but who have nonetheless contracted AIDS, most probably from the blood products used for their therapy. Several cases of suspected transmission of AIDS through transfusions have also been reported (JAMA, 1983, 249(12):1544-1545). Understandably, the reports of these cases have aroused both fear and resentment within the community of hemophiliacs and among many persons contemplating their own possible future need for blood transfusions. Even though the probability of harm to any given recipient of whole blood or antihemophilic factor is very slight, the magnitude of the harm when it occurs is great indeed.

In the long run, hemophiliacs and transfusion recipients will be best protected by either an effective screening test for the etiologic agent in AIDS or a method for inactivating that agent. In the interim, recipients of blood and blood products have little recourse but to rely on the good will of members of groups at high risk for contracting and transmitting AIDS. Newsletters oriented to the gay community and blood and plasma collection centers have urged members of high risk groups to refrain voluntarily from donating blood or selling plasma. Some centers have developed creative techniques for screening donors while maintaining donor anonymity.

Health professionals have moral obligations both to AIDS patients and to the other members of society. There are clearly tensions between these two sets of responsibilities. In fact, these tensions are reminiscent of venerable conflicts between the duties of primary caregivers and public health officials. If the irrational fears surrounding AIDS can somehow be allayed, I am convinced that health professionals will succeed in providing respectful and increasingly effective care for AIDS patients, while at the same time discovering new and creative ways to protect other members of society from the devastating impact of this disease.

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ASSOCIATION OF AIDS WITH A HISTORY OF BLOOD TRANSFUSION

Investigators at the CDC (Curran JW, Lawrence DN, Jaffe H, et al, N Engl J Med., 1984, 310:69-75) incriminate transfusion of blood and blood fractions as a risk factor for the acquisition of AIDS. Their evidence, while compelling, depends on an analysis that many may find difficult to follow. Their finding is that, although no blood donor with manifest AIDS was encountered, high-risk donors are uniformly found among those who have contributed blood to persons who subsequently developed AIDS. This finding is highly improbable under the null hypothesis which posits that the number of patients with transfusion-associated AIDS exposed to a high-risk donor would not be greater than the number expected by chance on the basis of the total number of donors to which each patient was exposed and the estimated prevalence of high-risk donors in the overall donor population. Although a simpler approach would be to compare the actual frequency of a history of blood transfusion among these AIDS patients with the frequency of transfusions in the general population, survey data that directly address the frequency of transfusion histories in the US population do not exist (J. Feldman, personal communication).

An indirect approach to estimating the expected frequency of transfusion histories can be made by combining available data from several sources. Friedman and colleagues (Friedman BA, Burns IL, Schork MA, et al: in Homburger HA and Batsakis JG (Eds): Clinical Laboratory Annual, Appleton Century Crofts, New York, 1982, 1:147-169) published a study showing the frequency of transfusions in the US using over one million hospital discharge records collected by the Commission on Professional and Hospital Activities. In another report, prepared by the National Center for Health Statistics (NCHS Series 10, No. 141, DHHS Publication (PHS) 82-1569, Table 15), estimates of the frequency of hospitalization, by age and sex, in the US population have been published. The product of values derived from these two studies can provide an estimate of the frequency with which any person or group of persons receives a transfusion. This value overlooks the rare transfusion administered to an ambulatory patient. The result will tend to overestimate the probability of a past transfusion history, because of the implicit assumption that no mortality difference exists between those who do and those who do not receive a transfusion. However, this approach should provide an upper limit to the number of AIDS patients who would be expected to give a history of blood

transfusions under the null hypothesis which assumes that there is no association between transfusions and AIDS.

The figures in Table 1 were very kindly provided by Dr. Friedman and his colleagues from unpublished tabulations in their investigation. Fitting a straight line by least squares analysis to the transfusion frequency as a function of the mid-point of each age interval made it possible to obtain by interpolation the first four transfusion frequencies for each sex (column 4 of Table 2). The fifth is taken directly from Table 1. The age and sex distribution

TABLE 1
PATIENTS DISCHARGED FROM HOSPITALS: AGE, SEX, AND TRANSFUSION HISTORY

	Percent Transfused	
Age	Male	Female
0-19	1.25	1.51
20-34	2.75	2.53
35-49	4.11	4.56
50-64	6.86	6.29
65 and over	9.55	9.72

TABLE 2
OBSERVED AND EXPECTED TRANSFUSION HISTORIES AMONG AIDS PATIENTS NOT BELONGING TO MAJOR RISK GROUPS

Age	No. AIDS Patients Reported to CDC	US Population Hospitalization Rate (%)	Hospital Transfusion Rate (%)	No. Cases Giving a Transfusion History	
				Expected	Observed
Males					
Under 25	4	7.0	2.175	0.03	1
25-34	19	7.4	3.278	0.23	1
35-44	19	9.5	4.439	0.40	2
45-64	29	18.2	6.181	1.59	12
65 and over	3	31.4	9.55	0.42	2
Totals	74			2.67	18
Females					
Under 25	8	21.0	2.313	0.19	0
25-34	23	21.9	3.305	0.82	3
35-44	7	13.8	4.349	0.21	0
45-64	15	16.9	5.916	0.74	7
65 and over	4	26.3	9.72	0.49	1
Totals	57			2.45	11
Grand Totals	131			5.12	29
				($p < 0.0001$)	

of the 131 adult cases of AIDS not belonging to any of the four major risk groups and having Pneumocystis carinii pneumonia are given in columns 1 and 2. These data, which were reported to CDC up to January 10, 1984, and the numbers of AIDS patients giving a history of transfusion within the past 5 years (column 6) were kindly provided by Dr. Curran. The expected number of AIDS patients giving a history of transfusion within 5 years (column 5) was computed according to the formula $E = N\ [1-(1-HT)^5]$ where E = expected number giving transfusion history, N = number of AIDS cases in the category (column 2), H = annual hospitalization rate (column 3), T = in-hospital transfusion rate (column 4).

The number of cases observed in each age-sex group exceeds expectation (columns 5 and 6), except where no cases were observed. Altogether, 29 cases were observed compared with an expectation of just over five. The strength and the consistency of the association speak for themselves. However, it is also of interest to note the value of Z for the standard statistical comparison of two rates or proportions. The result is 4.38, corresponding to a p value of less than 0.0001.

This analysis, using an entirely independent argument, appears to offer strong confirmation for the conclusions of Curran and colleagues.

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ARE SWINGERS AT RISK FOR AIDS?

Demographic studies traditionally have been of use in unraveling the mysteries of infectious disease processes. Such studies permit the construction of Venn diagrams which show the complex relationships of various factors in and to a disease. The peculiar demography of AIDS is evidenced in Venn diagrams showing relationships among homosexual preference, exposure to blood and blood products, geographical area, and so on. The diagrams can provide useful guides to laboratory research.

Most models designed to explain AIDS include both a mechanism by which immune responsiveness is diminished in affected individuals and an etiologic role for a new or altered strain of virus. The latter is invoked in part because AIDS is a new disease affecting mostly homosexual men, yet homosexual behaviors are not new (although they may now possibly involve greater degrees of promiscuity).

A number of the hypotheses concerning the etiology and spread of AIDS envision disease transmission through anal intercourse. However, no difference in the prevalence of anal intercourse has been reported between AIDS patients and matched healthy homosexual male controls (Darrow WW, Jaffe HW, Curran JW, Lancet, 1983, 2:160). In addition, anal intercourse is common as a heterosexual variant.

I suggest that a critical population to study in an effort to resolve some of the etiologic issues might be the group of so-called swingers who exist in precisely the geographic areas (New York, San Francisco, Los Angeles) where AIDS has its highest reported prevalence. Swingers have numerous heterosexual partners and may be as promiscuous as the most promiscuous male homosexuals

affected with AIDS. The "ground rules" for swingers usually exclude direct male-to-male contacts within the group but include heterosexual anal intercourse as a sexual variant. Most swingers are "tri"-sexuals (who will try anything). Drugs are usually frowned upon.

The swinger population is not epidemiologically closed: some of the male members engage in bisexual or homosexual activities outside the group in geographic areas where AIDS is prevalent. Clearly, if AIDS involves a specific venereal infection, the incidence of altered immunity should be demonstrable in swingers, particularly in those belonging to groups in which "exploration of the homosexual option" is encouraged. (In a study conducted in 1973-74, the only transmissible infections which members of this subculture reported as troublesome were trichomoniasis and angular conjunctivitis. More recently anxiety about the transmission of genital herpes has been reported. No major venereal disease(s) nor unusual ill health appear to have been reported.)

This group is small but is accessible for study by virture of its being organized. It does not appear to have been studied to date. A systematic study would provide data of use in constructing Venn diagrams for certain important elements which have been postulated as being contributory to both the spread and causation of AIDS. Among these would be exposure to numerous partners, practice of male-female anal intercourse, exposure to whole blood, exposure to seminal antigens from successive acts of coitus by more than one male with a single female, and transmission of an infectious agent through heterosexual contact. In addition, a study of immune competence in relation to these factors among multi-partnered individuals might throw light on a critical and underexplored side issue, that gender dysphoria itself assorts with some type of immune deficiency. Gender dysphoria is not a characteristic of the swinger subgroup.

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SEXUAL CONTACTS OF HOMOSEXUAL MEN WITH AIDS OR AIDS PRODROME

Epidemiologic evidence suggests that a transmissible agent in body secretions or blood is responsible for the spread of AIDS. We evaluated 18 sexual contacts of seven homosexual AIDS patients and seven homosexual men with the AIDS-related complex (ARC). All ARC patients had generalized lymphadenopathy, unexplained fever, weight loss, or malaise. Eleven of the 18 contacts had contact with AIDS patients and seven with the ARC patients. Of the 18, six had symptoms or signs and 12 were asymptomatic. The four groups of men were compared with 57 asymptomatic homosexual men with no known contact with AIDS patients. Lymphocyte counts, total T cells, T-cell subsets, skin test reactivity to five recall antigens, and immunoglobulin concentrations were recorded (Table).

AIDS and ARC patients showed T-cell lymphopenia, depletion of helper lymphocytes (OKT4), and markedly abnormal helper:suppressor (OKT4:OKT8) ratios. In symptomatic contacts (SXC), values for these parameters resembled those of AIDS and ARC patients. In contrast, asymptomatic contacts (ASC) showed values for lymphocytes, T cells, T-cell subsets, and OKT4:OKT8 ratios which were similar to those of controls. Anergy to five

skin test antigens was present in a high proportion of men with AIDS, ARC, and SXC compared to 18% of ASC and control patients. Hypergammaglobulinemia was most marked in the AIDS patients; it was more frequent in those with ARC, SXC, and ASC than in controls.

Only one of the 11 contacts of AIDS patients was himself symptomatic, while five of seven ARC contacts were symptomatic. Five of the sexual contacts have been re-examined 4-12 months after the initial evaluation. Three of these had contact with AIDS patients. Two of the three were initially asymptomatic and have remained free of symptoms. One contact initially had lymphadenopathy and weight loss. Four months later he had gained weight and showed a decrease in lymph node size. At follow-up, there were no changes in the lymphocyte counts, total T cells, or numbers of T-cell subsets in these men. Two of the three men had reversed OKT4:OKT8 ratios due to increases in the percentages and absolute numbers of OKT8 cells.

Two contacts of ARC patients initially had lymphadenopathy, fatigue, and weight loss. At follow-up, the lymphadenopathy persisted but other symptoms had improved. Both men initially and at follow-up showed a reversal of OKT4:OKT8 ratios and one developed lymphopenia.

The wife and 13-year-old son of a bisexual man with Pneumocystis carinii pneumonia have also been studied. Both were asymptomatic at the time of evaluation and had normal numbers of T cells and T-cell subsets.

In this study symptoms at the time of evaluation rather than contact history correlated with alterations in immune status.

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IMMUNOLOGIC MEASUREMENTS IN PATIENTS, CONTACTS, AND CONTROLS

	AIDS (7)*	ARC (8)	SXC (6)	ASC (12)	Controls (57)
Total Lymphocytes†	1420±442	2013±654	1635±533	2235±678	2430±828
OKT3	1167±410	1569±511	1220±137	1710±494	1951±691
OKT4	351±278	687±337	419±214	876±226	1142±542
OKT8	752±257	922±272	758±192	915±429	1051±402
(OKT4:OKT8)	0.47±0.31	0.72±0.26	0.57±0.35	1.15±0.60	1.13±0.52
Anergy‡	83	43	33	18	18
IgG§	2954±847	1454±502	1514±308	1384±472	1194±245
IgA	485±345	188±77	350±117	199±49	231±94
IgM	217±132	173±73	225±120	232±97	191±83

* (Number of patients). † Cells/mm³. ‡ % of patients. § µg/ml.

BONE MARROW CHANGES IN AIDS

Bone marrow aspirates from 14 patients with AIDS seen at the East Orange Veterans Administration Hospital between May 1982 and December 1983 were studied by light microscopy using routine Giemsa staining procedures. Three specimens were inadequate. Of the remaining 11, ten shared an unusual feature. These ten marrow preparations contained occasional mononuclear cells which had a thin rim of pale blue cytoplasm without granules. The nuclei were irregular in shape with cerebriform convolutions. The chromatin was clumped and a large nucleolus was easily identified. These cells were comparable in size to myelocytes.

The unusual cells accounted for about 0.5% of the nucleated marrow cells. Such cells were rarely seen, if at all, in marrow from non-AIDS patients.

These mononuclear cells are clearly not of either the myeloid or the erythroid series. Their cytoplasmic features are not typical of mature monocytes; nor are the nuclear features typical of lymphocytes. However, they could represent activated monocytes or lymphocytes.

This finding is probably not pathognomonic for AIDS. However it constitutes an additional finding to consider when evaluating patients suspected of having AIDS.

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AFRICAN EOSINOPHILIC BODIES IN VIVO IN TWO MEN WITH KAPOSI'S SARCOMA AND AIDS

Histologic analyses were performed on biopsy specimens from cutaneous Kaposi's sarcoma (KS) tumors of two men with AIDS. One patient was a 51-year-old, promiscuous, bisexual, black American man with extensive lesions of KS on the trunk, bilateral parotid swelling, and Whipple's-like intestinal disease. The other patient was a 42-year-old, promiscuous, homosexual, Mexican-American man with multiple cutaneous lesions of KS and *Pneumocystis carinii* pneumonia.

With routine hematoxylin-eosin staining procedures, pink-stained, variably sized, coccoid-shaped, intracellular and extracellular eosinophilic bodies were seen. Such forms are commonly observed in histologic analyses of specimens taken from African cases of KS (Murray JF, Lothe F: Acta Unio Int Cancer, 1962, 18:413-428). The eosinophilic bodies can be identified in sections of KS specimens stained with Gram's stain or the Giemsa stain, as previously noted by pathologists in Africa (Lee FD: J Clin Pathol., 1968, 21:119-128). In this study, these forms were best identified in Fite (acid-fast) stained sections using the oil-immersion lens (×1000).

The exact nature of the eosinophilic bodies is unknown. Such structures have been reported in other types of tumors (Ibid: 119-128) and are thought to be related to Russell bodies. They are very similar to and may be identical to the acid-fast coccoid forms and Russell bodies detected previously in various forms of cancer and in KS and AIDS (Cantwell AR Jr: Growth, 1982, 46:331-336; Growth, 1983, 47:129-134; Cutis, 1983, 32:58-68). These eosinophilic bodies may be directly related to the cell wall deficient forms of bacteria

which can be demonstrated in vivo. They may also be related to the elusive and mysterious "agent" of KS and AIDS.

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CHEMOIMMUNOTHERAPY PROTOCOL FOR EPIDEMIC KAPOSI'S SARCOMA

A protocol has been initiated at the Rita and Stanley H. Kaplan Cancer Center at New York University to evaluate the effects of concurrent therapies with recombinant alpha-2 interferon (IFN) (Schering Corp., Kenilworth, NJ) and etoposide (VP-16) in the treatment of patients with the epidemic form of Kaposi's sarcoma (EKS).

The extent of disease in patients will be determined according to the classification of Krigel et al. (Krigel RL, Laubenstein LJ, Muggia FM: Cancer Treat Rep., 1983, 67:531-534) and only those in stages III and IV subsets A and B will be eligible. All patients must not have received prior systemic therapy and must not have current opportunistic infections.

Escalating doses of both IFN (15-50 × 10^6 U, days 1-5) and VP-16 (100-150 mg/m^2, days 1-3) will be administered intravenously in 21 day cycles for a total of 4-6 cycles.

After completion of this induction phase, patients in whom a complete response (CR) is achieved will receive either maintenance therapy or no further therapy. The effect of IFN on the duration of CR will be evaluated. Other effects of the therapeutic protocol which will be evaluated include effects on immune functioning, on the subsequent development of opportunistic infections and classification of these infections, and on overall survival. Patients showing partial responses (PR will be measured as reduction in the size of lesions by more than 50% in cross-sectional area) following initial therapy will receive further IFN therapy; observations will then be made on the ability of IFN to convert PR into CR.

It is hoped that the combination therapy, aimed at both immune modulation and anti-neoplastic effects, will yield better results than can be obtained using each agent alone. Both IFN (Krown SE, Real FX, Cunningham-Rundles S, et al: N Engl J Med., 1983, 308:1071-1076; Krown SE, Real FX, Cunningham-Rundles S, et al: N Engl J Med., 1983, 309:923-924; Volberding P, Gottlieb M, Rothman J, et al: Proc Am Soc Clin Oncol., 1983, 2:53) and VP-16 (Laubenstein LJ, Krigel RL, Hymes KB, et al: Proc Am Soc Clin Oncol., 1983, 2:228) have known activities in EKS when given as single therapeutic agents.

The study was begun on January 1, 1984. Further information concerning entry into and conduct of the study can be obtained from Drs. R. L. Krigel or C. Odajnyk at (212) 340-7226 or (212) 340-6485.

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A PILOT STUDY OF IN VIVO IMMUNOMODULATION BY ISOPRINOSINE IN AIDS AND AIDS-RELATED COMPLEX

The immunomodulatory effects of isoprinosine were studied in vivo in nine patients with AIDS and AIDS-related complex. All patients had been stable clinically for at least 4 weeks before

the initiation of therapy. Isoprinosine (Newport Pharmaceuticals International, Inc., Newport Beach, CA) was administered in doses of 4 gm/day for 4 weeks to patients who had given written informed consent. Blood samples were drawn just before treatment was started, on the 14th and 28th days of therapy, and 14 days after discontinuation of the drug. T cells were analyzed phenotypically for OKT4 and OKT8 markers. Lymphocyte proliferative responses to mitogens were quantitated before therapy, on the 28th day of therapy, and 14 days after the discontinuation.

There was no significant association of isoprinosine treatment and alteration of OKT4:OKT8 ratio in any subject. There were no significant enhancements of lymphocyte proliferative responses to phytohemagglutinin (PHA), concanavalin A (Con A), and pokeweed mitogen (PWM) in five patients with AIDS.

The mean lymphocyte proliferative responses to PHA in four patients with AIDS-related complex increased from 39,109(±35,442) cpm to 64,546(±35,307) cpm after 28 days of treatment and then decreased to 15,481(±10,096) cpm 14 days after discontinuation. Similarly, the mean lymphocyte proliferative responses to Con A in the patients with AIDS-related complex increased from 10,681 (±8,245) cpm to 60,478(±33,119) cpm after 28 days of therapy ($p < 0.05$) and decreased to 12,418(±10,395) cpm 14 days after discontinuation of the drug. The proliferative response to PHA in one of four patients with AIDS-related complex increased markedly after 28 days of treatment with isoprinosine, while the Con A response was enhanced in all four.

Further trials appear warranted with isoprinosine in a larger group of patients with AIDS-related complex to establish immunologic effectiveness, appropriate dosages, and mechanism(s) of immune enhancement.

M. E. Grieco, M. M. Reddy, M. L. Moriarty, D. Manvar, and K. K. Ahuja. R. A. Cooke Institute of Allergy, St. Luke's/Roosevelt Hospital Center, New York, New York 10019.

UPCOMING AIDS MEETING

Conference on AIDS: Diagnosis and Management. A Conference Designed for the Physician in Primary Care.

June 8-10, 1984
Warwick Post Oak Hotel
Houston, Texas

Information will be presented on the etiology and epidemiology of AIDS. Clinical presentations, diagnostic procedures (especially immunologic methods), treatments, and complications associated with AIDS and KS will be reviewed. The infectious complications and treatment protocols using chemotherapy, immunotherapy, and immune restoration will be emphasized.

Speakers: J. Knox, D. Schottenfeld, D. McMurrey, C. Ericsson, V. Fainstein, J. L. Melnick, C. Noonan, I. Shivitiz, P. Volberding, F. Hagemeister, C. Lane, A. Rios, C. Plager, M. Grieco, Y. Patt, P. W. Mansell, G. Newell, and E. Hersh.

Contact:
Office of Conference Services
M. D. Anderson Hospital
and Tumor Institute
Box 131, 6723 Bertner Avenue
Houston, Texas 77030
(713) 792-2222 or
University of Texas Health
Science Center at Houston
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(713) 792-4671

AIDS CASES REPORTED TO THE CENTERS FOR DISEASE CONTROL AS OF April 2, 1984

UNITED STATES CASES

DISEASE	CASES	PERCENT OF TOTAL	DEATHS	PERCENT DEAD
KS without PCP	989	25.0	243	24.6
PCP without KS	2042	51.6	975	47.7
Both KS and PCP	266	6.7	167	62.8
OI without KS or PCP	657	16.6	338	51.4
TOTAL	3954	100.0	1723	43.6

KS = Kaposi's sarcoma
OI = Opportunistic infections
PCP = Pneumocystis carinii pneumonia

	MALES		FEMALES		TOTAL	
RISK GROUPS*	CASES	% OF TOTAL	CASES	% OF TOTAL	CASES	%
Homosexual or bisexual	2819	76.6	0	0.0	2819	71.3
IV drug user	547	14.9	150	55.1	697	17.6
Haitian	141	3.8	24	8.8	165	4.2
Hemophiliac	28	0.8	0	0.0	28	0.7
No apparent risk group or unknown	147	4.0	98	36.0	245	6.2
TOTAL	3682	100.0	272	100.0	3954	100.0

* The risk groups listed are hierarchically ordered; cases with multiple risk factors are tabulated only in the risk group listed first.

INSTRUCTIONS FOR AUTHORS CONTRIBUTING TO THE AIDS MEMORANDUM

Content: Articles published in the AIDS Memorandum must have obvious relevance to AIDS. They can describe clinical or experimental findings. Letters and other types of commentary are also welcome. All manuscripts should be typed double spaced.

References: References should be integrated into the text in parentheses. Each citation should include the names of up to three authors, the journal title, the year of publication, volume and issue numbers, and inclusive page numbers. Citations from books should include the names of up to three authors, book title, editor(s), publisher, publisher's location, year of publication, and relevant page numbers.

Tables and Figures: Whenever possible, data should be organized into tables. Figures should be clear and no wider than 3½ inches.

Announcements of Meetings: Announcements of upcoming AIDS meetings should include meeting title, location, and date and the name, address, and telephone number of the organizer of the meeting.

Further Information: For further information call the AIDS Memorandum office at (301) 496-9537.

Mailing Instructions: Manuscripts for the AIDS Memorandum should be sent to this address:

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